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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,389	07/24/2003	Tetsuo Hayashi	1/1379US	9782

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MICHAEL P. MORRIS
BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877-0368

EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,389	HAYASHI ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Humera N. Sheikh
Primary Examiner
TC-1600

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/22/03; 12/18/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Information Disclosure Statements(IDS) filed 09/22/03 and 12/18/03 is acknowledged.

Claims 1-34 are pending in this action. Claims 1-34 are rejected.

Inventorship

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen *et al.* (WO 99/32125) in view of Abu-Izza *et al.* (U.S. Pat. No. 6,733,781 B2).

The instant invention is drawn to a pharmaceutical composition comprising:

(a) an antihistaminically-effective amount of epinastine or a pharmaceutically acceptable salt thereof;

(b) a decongestant-effective amount of pseudoephedrine or a pharmaceutically acceptable salt thereof;

(c) methylephedrine or a pharmaceutically acceptable salt thereof; and

(d) a pharmaceutically acceptable carrier or excipient,

wherein the composition does not comprise Belladonna.

Jensen *et al.* ('125) teach a layered oral pharmaceutical composition comprising an effective amount of an antihistamine, such as epinastine or a pharmaceutically acceptable salt thereof in combination with an effective amount of a decongestant, such as pseudoephedrine along with pharmaceutically acceptable excipients and carriers for the treatment of conditions which include sneezing, itching runny nose, nasal congestion, redness of the eye, allergic rhinitis,

common colds, sinusitis and various other respiratory and skin diseases (see reference page 1, lines 1-20); (pg. 2, lines 1-35); (pg. 9, lines 1-36); (pg. 13, lines 15-20); (pg. 14, lines 9-29).

Jensen *et al.* teach at page 9, lines 25-33 that the compositions may be formulated in sustained release form to provide the rate controlled release of any one or more of the components or active ingredients to optimize the therapeutic effects, (*i.e.*, leukotriene antagonism, antihistaminic and the like).

Suitable dosage forms for sustained release include *layered tablets* containing layers of varying disintegration rates or controlled release polymeric matrices impregnated with the active components and shaped in tablet form or capsules containing such impregnated or encapsulated porous polymeric matrices. Capsules can have an enclosure made of methyl cellulose, polyvinyl alcohols, or denatured gelatins or starch. The capsules may also contain dyes, opaquing agents, plasticizers and preservatives (pg. 9. line 25 – pg. 10, line 22).

Jensen *et al.* teach that the amount of epinastine that can be employed in a unit dosage form can range from about 1 to about 20 mg (instant range is 2mg to 25 mg/tablet) (see page 5, lines 19-20). While Jensen *et al.* do not teach the instantly claimed amount of pseudoephedrine (10 to 300 mg/tablet), the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicants have not demonstrated any surprising or unexpected results, which accrue from the instant amounts of pseudoephedrine. The prior art clearly recognizes and teaches a layered oral

pharmaceutical composition comprising an effective amount of an antihistamine (*i.e.*, epinastine) in combination with an effective amount of a decongestant (*i.e.*, pseudoephedrine) along with pharmaceutically acceptable excipients. The decongestant (*i.e.*, pseudoephedrine) aids in the treatment of diseases of the respiratory tract and/or concomitant symptoms and therefore is provided in effective amounts. Furthermore, it is deemed obvious to one of ordinary skill in the art to determine suitable and effective ranges of active ingredient through the use of routine or manipulative experimentation to obtain the best possible results, as these are indeed variable parameters attainable within the art.

Jensen *et al.* teach and recognize layered tablet formulations that are prepared by compression of mixtures or granulations obtained by wet granulation, dry granulation or by compaction (see for instance, page 9, line 35 – pg. 10, line 16).

Jensen *et al.* do not teach methylephedrine.

Abu-Izza *et al.* ('781) teach fast dissolving tablets comprising active agents such as antihistamines and decongestants. Specific active agents disclosed that are common allergy medications include antitussive/anti-asthmatic agents such as methylephedrine (hydrochloride) (see reference column 5, lines 50-52); (col. 6, lines 63-65); and Example 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the antitussive/anti-asthmatic agent, methylephedrine taught by Abu-Izza *et al.* within the decongestant/antihistamine composition of Jensen *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Abu-Izza e*t al.* teach methylephedrine and teach that the medicament is a suitable and effective

medication used for common allergies. The expected result would be an improved decongestant/antihistamine combination composition for the effective treatment of seasonal disorders and diseases.

With regards to the instantly claimed amount of methylephedrine (10 to 240 mg/tablet), the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicants have not demonstrated any surprising or unexpected results, which accrue from the instant amounts of methylephedrine. The prior art clearly recognizes and teaches tablet compositions comprising the same active ingredient, methylephedrine, used for the same field of endeavor as the Applicant to treat the same problems (*i.e.*, common allergies). Furthermore, it is deemed obvious to one of ordinary skill in the art to determine suitable and effective ranges of active ingredient through the use of routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art.

Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vilkov *et al.* (US Pat. No. 5,807,579) in view of Jensen *et al.* (WO 99/32125) and further in view of Abu-Izza *et al.* (U.S. Pat. No. 6,733,781 B2).

The instant invention is drawn to a pharmaceutical composition comprising:

(a) an antihistaminically-effective amount of epinastine or a pharmaceutically acceptable salt thereof;

(b) a decongestant-effective amount of pseudoephedrine or a pharmaceutically acceptable salt thereof;

(c) methylephedrine or a pharmaceutically acceptable salt thereof; and

(d) a pharmaceutically acceptable carrier or excipient,

wherein the composition does not comprise Belladonna.

Vilkov *et al.* ('579) teach a pharmaceutical tablet for oral administration comprising a therapeutically effective amount of a decongestant, such as pseudoephedrine or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of a second drug, which is an *antihistamine*, whereby the tablet provides for an extended release of pseudoephedrine and an immediate release of the antihistamine drug. In another embodiment, the second active drug (*i.e.*, antihistamine) may be spray-coated on the outside of the tablet to provide an immediate release layer (col. 6, lines 15-24). The pharmaceutical tablet is formulated without the addition of a leukotriene antagonist (see reference column 1, lines 60-67); (col. 2, lines 1-49); (col. 3, lines 26-52); (col. 4, lines 33-42); (col. 5, lines 15-55).

In a preferred embodiment, the extended-release pellets of the invention comprise a therapeutically effective amount of the active ingredient, pseudoephedrine. The pellets comprise a polymer coating, which controls release of the pseudoephedrine (col. 3, line 55 – col. 4, line 1). The polymer coating comprises water-soluble and water-insoluble polymer. Suitable water-soluble polymers taught include hydroxypropyl cellulose and hydroxypropyl methylcellulose

(col. 4, lines 8-25). This teaching meets Applicant's limitations of claim 20, which recite pseudoephedrine in a matrix of a swellable hydrophilic polymer.

The tablet composition comprises carriers and excipients, that are well known in the art, such as lubricants, fillers, plasticizers, binders, disintegrants and the like (col. 3, line 26 – col. 4, line 42).

Example 1 at columns 5-6 demonstrates a decongestant/antihistamine composition and method for preparing. As shown in the table at column 6, pseudoephedrine hydrochloride is provided at a dosage concentration of 10 mg/tablet. This amount meets the instant range of 10 to 300 mg/tablet of pseudoephedrine or a pharmaceutically acceptable salt recited in instant claim 5. The antihistamine (terfenadine) is provided at a dosage concentration of 60 mg/tablet. While this range lies outside of the instantly claimed range of antihistamine (epinastine salt) of 2 to 25 mg/tablet, it is noted that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicants have not demonstrated any surprising or unexpected results, which accrue from the instant amounts of antihistamine, particularly epinastine salt. Applicants have also not shown any unexpected results, which accrue from the amounts claimed in instant claim 2. The prior art teaches a layered oral pharmaceutical composition comprising a therapeutically effective amount of a decongestant, pseudoephedrine or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of a second drug, which is an antihistamine, whereby the tablet

provides for an extended release of pseudoephedrine and an immediate release of the antihistamine drug in combination with pharmaceutically acceptable excipients. Furthermore, it is deemed obvious to one of ordinary skill in the art to determine suitable and effective ranges of active ingredient through the use of routine experimentation to obtain an optimal outcome.

Vilkov *et al.* teach layered tablet formulations that are prepared by direct compression of the active ingredient, particularly antihistamine (see for instance, column 5, line 50-67).

With respect to the instant method of claim 34, which recite a 'method for treating allergic rhinitis, seasonal allergic conjunctivitis, allergic rhinitis, allergic congestion of Eustachian tubes or other diseases of allergic origin treated using antihistamine and decongestant drugs' it is the position of the Examiner that the instant methods of treating are deemed obvious given the teachings of Vilkov *et al.* Vilkov *et al.* explicitly teach oral, layered tablet compositions comprising sustained release pseudoephedrine in combination with an immediate release antihistamine drug, and therefore one ingesting the tablet composition of Vilkov *et al.* would be able to effectively treat and alleviate allergic and seasonal disorders and conditions and would be capable of treating various symptoms of the allergic disorders, such as the common cold or flu. Therefore, given the teachings of Vilkov *et al.,* to formulate compositions having decongestants with antihistamines, the instant methods of treatment would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Vilkov *et al.* teach the concept of combining a decongestant agent (pseudoephedrine) with a second antihistaminic agent in combination with acceptable carriers and excipients, wherein the decongestant is in extended release form and the antihistamine is provided in an immediate release form as instantly claimed.

Vilkov *et al.* teach an antihistamine in combination with a decongestant (pseudoephedrine). Vilkov *et al.* do not teach *epinastine* as the particular antihistamine.

Jensen *et al.* ('125) teach a layered oral formulation comprising a decongestant, such as pseudoephedrine in combination with antihistamines, whereby suitable antihistamines include *epinastine*, cetirizine, astemizole and the like. The layered formulation provides for the treatment of respiratory conditions, such as seasonal allergic rhinitis, perennial allergic rhinitis, common colds, sinusitis and symptoms associated with allergic asthma (see reference page 1, line 6 – pg. 3, line 12) and Abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the antihistamine, epinastine of Jensen *et al.* within the decongestant/antihistamine composition of Vilkov *et al.* because Jensen *et al.* teach a layered pharmaceutical composition that comprises antihistamines in combination with a decongestant and Jensen *et al.* teach that epinastine is a suitable and effective antihistamine that enhances the overall efficacy of the composition and aids in the treatment of diseases of the respiratory tract, such as seasonal allergic rhinitis, perennial allergic rhinitis, common colds, sinusitis and symptoms associated with allergic asthma. The expected result would be an antihistamine/decongestant tablet formulation for the beneficial and effective treatment of allergic diseases and disorders, as similarly desired by Applicant(s).

The teachings of Vilkov *et al.* and Jensen *et al.* are delineated above.

They do not teach methylephedrine.

Abu-Izza *et al.* ('781) teach fast dissolving tablets comprising active agents such as antihistamines and decongestants. Specific active agents disclosed that are common allergy medications include antitussive/anti-asthmatic agents such as methylephedrine (hydrochloride) (see reference column 5, lines 50-52); (col. 6, lines 63-65); and Example 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the antitussive/anti-asthmatic agent, methylephedrine taught by Abu-Izza *et al.* within the decongestant/antihistamine composition of Vilkov *et al.* or alternatively, Jensen *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Abu-Izza *et al.* teach methylephedrine and teach that the medicament is a suitable and effective medication used for common allergies. The expected result would be an improved decongestant/antihistamine combination composition for the effective treatment of seasonal disorders and diseases.

With regards to the instantly claimed amount of methylephedrine (10 to 240 mg/tablet), the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicants have not demonstrated any surprising or unexpected results, which accrue from the instant amounts of methylephedrine. The prior art clearly recognizes and teaches tablet compositions comprising the same active ingredient, methylephedrine, used for the same field of endeavor as

the Applicant to treat the same problems (*i.e.*, common allergies). Furthermore, it is deemed obvious to one of ordinary skill in the art to determine suitable and effective ranges of active ingredient through the use of routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable by the skilled artisan.

Thus, given the teachings of the prior art above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

October 01, 2006

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